Claims

I claim:

1. A method for detecting or determining the interaction of a first CFTR polypeptide with a second CFTR polypeptide, said method comprising:

(a) providing a first polynucleotide encoding a fusion protein comprising all or a portion of a first CFTR polypeptide and a DNA binding domain of a transcriptional activator that can bind to a site on a detectable gene;

(b) providing a second polynucleotide encoding a fusion protein comprising all or a portion of a second CFTR polypeptide and a transcriptional activation domain of a transcriptional activator that can activate transcription of said detectable gene;

(c) incorporating said first and second polynucleotide into a host cell comprising said detectable gene wherein transcription of said detectable gene is under control of said transcriptional activator;

(d) expressing said polynucleotide encoding said first CFTR polypeptide and said second CFTR polypeptide under conditions in which said detectable gene is expressed when said first CFTR polypeptide and said second CFTR polypeptide interact; and

(e) detecting transcription of said detectable marker gene or expression of the gene product of said detectable gene.

2. The method according to claim 1, wherein said host cell is a yeast cell.

3. The method according to claim 2, wherein said yeast cell is *Saccharomyces*.

4. The method according to claim 1, wherein the host cell is a mammalian cell.

5. The method according to claim 1, wherein said CFTR polypeptide is a mammalian CFTR polypeptide.

6. The method according to claim 1, wherein said CFTR polypeptide comprises amino acid residue 351 through 650 of the human CFTR protein sequence.

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7. The method according to claim 1, wherein said detectable gene is selected from the group consisting of lacZ, *LEU2* and *HIS3*.

8. The method according to claim 1, wherein said DNA binding domain comprises the DNA binding domain of GAL4 protein.

9. The method according to claim 1, wherein said transcriptional activation domain comprises the transcriptional activation domain of GAL4 protein.

10. The method according to claim 1, wherein said CFTR polypeptides are mutant CFTR polypeptides.

11. The method according to claim 1, wherein said CFTR polypeptide comprises a mutation in the first nucleotide binding domain (NBD1).

12. The method according to claim 10, wherein said mutant CFTR polypeptide contains a ΔF508 mutation.

13. The method according to claim 1, wherein said CFTR polypeptide is a wild type CFTR polypeptide.

14. A method of identifying a compound that facilitates interaction of CFTR polypeptides, said method comprising:

(a) contacting a host cell with said compound, wherein said host cell comprises a polynucleotide encoding a fusion protein comprising all or a portion of a first CFTR protein and a DNA binding domain of a transcriptional activator that can bind to a site on a detectable gene, and a polynucleotide encoding a fusion protein comprising all or a portion of a second CFTR polypeptide and a transcriptional activation domain of a transcriptional activator that can activate transcription of a detectable gene, wherein said host cell further comprises said detectable gene wherein transcription of said detectable gene is under control of said transcriptional activator,

wherein said first and second CFTR polypeptides comprise a mutation that reduces or

prevents interaction of said fusion proteins;

(b) expressing said polynucleotide encoding said first CFTR polypeptide and said second CFTR polypeptide under conditions in which said detectable gene is expressed when said first CFTR polypeptide and said second CFTR polypeptide interact; and,

(c) determining whether said detectable gene is expressed in said host cell at a level greater than the level of expression observed in said host cell in the absence of said compound.

15. The method according to claim 14, wherein said host cell is a yeast cell.

16. The method according to claim 15, wherein said yeast cell is *Saccharomyces*.

17. The method according to claim 14, wherein the host cell is a mammalian cell.

18. The method according to claim 14, wherein said CFTR polypeptide is a mammalian CFTR polypeptide.

19. The method according to claim 14, wherein said CFTR polypeptide comprises amino acid residue 351 through 650 of the human CFTR protein sequence.

20. The method according to claim 14, wherein said detectable gene is selected from the group consisting of lacZ, *LEU2* and *HIS3*.

21. The method according to claim 14, wherein said DNA binding domain comprises the DNA binding domain of GAL4 protein.

22. The method according to claim 14, wherein said transcriptional activation domain comprises the transcriptional activation domain of GAL4 protein.

23. The method according to claim 14, wherein said CFTR polypeptides are mutant CFTR polypeptides.

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24. The method according to claim 14, wherein said CFTR polypeptide comprises a mutation in the first nucleotide binding domain (NBD1).

25. The method according to claim 23, wherein said mutant CFTR polypeptide contains a ΔF508 mutation.

26. The method according to claim 14, wherein said compound is present in a plant and said host cells is contacted with a tissue sample from said plant.

27. The method according to claim 26, wherein said tissue sample is a leaf disc from said plant.

28. The method according to claim 14, wherein said host cell is contacted with a sample present or absorbed on a filter paper disc.

29. The method according to claim 14, wherein increased growth of said host cells is used for determining whether said detectable gene is expressed in said host cells at a level greater than the level of expression observed in said host cells in the absence of said compound.

30. The method according to claim 14, wherein said CFTR polypeptide is a wild type CFTR polypeptide.

31. The method according to claim 14, wherein said compound is selected from the group consisting of a polypeptide or a biologically active fragment thereof, an antibody or antigen binding fragment thereof, and a polynucleotide.

32. A method for detecting or determining the interaction of a first CFTR polypeptide with a second CFTR polypeptide, said method comprising (a) providing a fusion protein comprising all or a portion of a first CFTR protein and a DNA binding domain of a transcriptional activator that can bind to a site on a detectable marker gene; (b) providing a second fusion protein comprising all or a portion of a second CFTR

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polypeptide and a transcriptional activation domain of a transcriptional activator that can activate transcription of the detectable marker gene; (c) contacting said first fusion protein and said second fusion protein under conditions where if said first fusion protein and said second fusion protein interact then said interaction causes said transcriptional activation domain to activate transcription of said detectable marker gene; and (d) detecting transcription of said detectable marker gene or expression of the gene product of said detectable marker gene.

33. The method according to claim 32, wherein said host cell is a yeast cell.

34. The method according to claim 33, wherein said yeast cell is *Saccharomyces*.

35. The method according to claim 32, wherein the host cell is a mammalian cell.

36. The method according to claim 32, wherein said CFTR polypeptide is a mammalian CFTR polypeptide.

37. The method according to claim 32, wherein said CFTR polypeptide comprises amino acid residue 351 through 650 of the human CFTR protein sequence.

38. The method according to claim 32, wherein said detectable gene is selected from the group consisting of lacZ, *LEU2* and *HIS3*.

39. The method according to claim 32, wherein said DNA binding domain comprises the DNA binding domain of GAL4 protein.

40. The method according to claim 32, wherein said transcriptional activation domain comprises the transcriptional activation domain of GAL4 protein.

41. The method according to claim 32, wherein said CFTR polypeptides are mutant CFTR polypeptides.

42. The method according to claim 32, wherein said CFTR polypeptide comprises a mutation in the first nucleotide binding domain (NBD1).

43. The method according to claim 41, wherein said mutant CFTR polypeptide contains a ΔF508 mutation.

44. The method according to claim 32, wherein said CFTR polypeptide is a wild type CFTR polypeptide.

45. A host cell comprising a polynucleotide encoding a fusion protein comprising all or a portion of a first CFTR protein and a DNA binding domain of a transcriptional activator that can bind to a site on a detectable gene and a polynucleotide encoding a fusion protein comprising all or a portion of a second CFTR protein and a transcriptional activation domain of a transcriptional activator that can activate transcription of said detectable gene.

46. The host cell according to claim 45, wherein said host cell is a yeast cell.

47. The host cell according to claim 46, wherein said yeast cell is *Saccharomyces*.

48. The host cell according to claim 45, wherein the host cell is a mammalian cell.

49. The host cell according to claim 45, wherein said CFTR polypeptide is a mammalian CFTR polypeptide.

50. The host cell according to claim 45, wherein said CFTR polypeptide comprises amino acid residue 351 through 650 of the human CFTR protein sequence.

51. The host cell according to claim 45, wherein said detectable gene is selected from the group consisting of lacZ, *LEU2* and *HIS3*.

52. The host cell according to claim 45, wherein said DNA binding domain comprises the DNA binding domain of GAL4 protein.

53. The host cell according to claim 45, wherein said transcriptional activation domain comprises the transcriptional activation domain of GAL4 protein.

54. The host cell according to claim 45, wherein said CFTR polypeptides are mutant CFTR polypeptides.

55. The host cell according to claim 45, wherein said CFTR polypeptide comprises a mutation in the first nucleotide binding domain (NBD1).

56. The host cell according to claim 54, wherein said mutant CFTR polypeptide contains a ΔF508 mutation.

57. The host cell according to claim 45, wherein said CFTR polypeptide is a wild type CFTR polypeptide.

58. A method for treating a person afflicted with cystic fibrosis, said method comprising providing or administering to said person an effective amount of a compound that restores or enhances dimerization of CFTR polypeptide or the exit of CFTR polypeptide from endoplasmic reticulum of a cell.

59. The method according to claim 58, wherein said compound is provided by gene therapy of said person.